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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,311	12/22/2004	Roland Martin	4239-64111-05	9128

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EXAMINER	
HISSONG, BRUCE D	
ART UNIT	PAPER NUMBER
1646	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,311	MARTIN ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 6 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,8-14,16,17 and 19-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,8-14,16,17 and 19-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. Applicants response to the office action mailed on 8/11/2006, including arguments/remarks and amendments to the claims, was received on 12/18/2006 and has been entered into the record.

2. In the response received on 12/18/2006, the Applicants have cancelled claims 2, 7, 15, and 18, and added new claims 21-26. Claims 1, 3-6, 8-14, 16-17, and 19-26 are therefore pending and the subject of this office action.

Specification

Objection to the specification for improperly identified trademarks, as set forth on page 2 of the office action mailed on 8/11/2006, is *maintained* for reasons of record. The Applicants response received on 12/18/2006 did not address this issue, and therefore the objection is maintained.

Claim Objections

1. Objection to claim 14, as set forth on page 2 of the office action mailed on 8/11/2006, is *maintained* for reasons of record. The Applicants response received on 12/18/2006 did not address this issue, and therefore the objection is maintained.

2. Objection to claim 20, as set forth on page 3 of the office action mailed on 8/11/2006, is *maintained* for reasons of record. The Applicants response received on 12/18/2006 did not address this issue, and therefore the objection is maintained.

3. The Examiner suggests the syntax of claim 20 can be improved by amending the claim to recite "administering to the subject" instead of "administering to a the subject".

4. The Examiner suggest the syntax of new claim 21 can be improved by amending the claim to read "administering to a subject" rather than "administering to a the subject". Furthermore, the Examiner suggests the syntax of the claim can be improved by amending the claim to read "for two weeks and then monthly, and administering to the subject".

Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Rejection of claims 1, 3-6, 8-14, 16-17, and 19 under 35 USC § 112, first paragraph, regarding lack of enablement for a method of treating any autoimmune disease other than multiple sclerosis, and administering any interleukin (IL)-2 receptor (IL-2R) antagonist other than anti-IL-2R antibodies, as set forth on pages 3-5 of the prior office action mailed on 8/11/2006, is *withdrawn* in response to Applicant's amendments to the claims to specifically recite a method of treating a subject that has multiple sclerosis, and to specifically recite administration of an antibody that specifically binds the IL-2 receptor.

Claim Rejections - 35 USC § 112, first paragraph – written description

Rejection of claims 1, 3-6, 8-14, 16-17, and 19 under 35 USC § 112, first paragraph, regarding lack of written description for any other IL-2R antagonist other than anti-IL-2R antibodies, as set forth on page 5 of the prior office action mailed on 8/11/2006, is withdrawn in response to Applicant's amendments to the claims to specifically recite administration of an antibody that specifically binds the IL-2 receptor, and the disclosure in the specification of several anti-IL-2R antibodies.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Rejections withdrawn

1. Rejection of claim 11 under 35 USC § 112, second paragraph, as being indefinite in regards to claimed trademarks, as set forth on page 6 of the prior office action mailed on 8/11/2006, is *withdrawn* in response to Applicant's amendments to the claim to delete trademarked products.

2. Rejection of claims 1, 3-6, 8-14, 16-17, and 19-20 under 35 USC § 112, second paragraph, as being indefinite regarding the metes and bounds of a "therapeutically effective combination" as set forth on page 6 of the prior office action mailed on 8/11/2006, is withdrawn in response to the Applicants' amendments to the claims to recite "a therapeutically effective amount of interferon beta" and "a therapeutically effective amount of an antibody that specifically binds the interleukin-2 receptor". Furthermore, the Applicants argue that the claims have been amended to read only on methods of treating multiple sclerosis, and that a person of ordinary skill in the art could readily identify symptoms of multiple sclerosis, and specific parameters to be detected are set forth in the specification, and thus the claims are not indefinite in regards to treating multiple sclerosis, or in regards to "a therapeutically effective combination". These arguments have been fully considered and are persuasive.

Rejections maintained/necessitated by amendment

3. Claims 9 and 17 *remain rejected*, and amended claims 12 and 20, as well as new claim 21, are also rejected under 35 USC § 112, second paragraph, as being indefinite in regard to claimed trademarks, as set forth on page 6 of the prior office action mailed on 8/11/2006. The Applicants' response received on 12/18/2006 does not address this issue, and it is noted that trademarks appear in these claims.

4. Claims 6, 9, 12, and 14 recite the limitation "the interleukin-2 receptor antagonist". There is insufficient antecedent basis for this limitation in the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Rejection of claim 20 under 35 USC § 102(b) as being anticipated by the "Study of Zenepax" document, as set forth on pages 6-7 of the office action mailed on 8/11/2006, is *withdrawn*. In the response received on 12/18/2006, the Applicants argue that claim 20 has been amended to depend from claim 1, and that the "Study of Zenepax" document does not teach the limitations of claim 1.

The Examiner notes that although claim 20 has not in fact been amended to depend from claim 1, it has been amended such that the claim now reads on a method of treating multiple sclerosis, wherein said method comprises administration of daclizumab, and further comprises administration of interferon-beta-1b (IFN-β-1b), which is not taught by the "Study of Zenepax" document. Accordingly, the rejection is withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-6, 8-14, 16-17, and 19 *remain rejected*, and amended/new claims 20-26 are also rejected, under 35 USC § 103(a) as being obvious in view of the combination of the "Study of Zenepax" document, Khoury *et al* ("Khoury"), Paty *et al* ("Paty"), and Jacobs *et al* ("Jacobs"), as set forth on pages 7-9 of the office action mailed on 8/11/2006. The claims of the instant application are drawn to a method of treating multiple sclerosis, wherein said method comprises administering IFN-β and an IL-2R antagonist. The claims are further drawn to administration of IFN-β-1a and IFN-β-1b, and in some embodiments, specifically recites administration of Betaseron (IFN-β-1b). The claims are also further drawn to administration of the anti-Tac antibody daclizumab or Zenapax.

The "Study of Zenapax" disclosure describes a clinical trial wherein the IL-2R antagonist Zenepax, which is taught by the specification to be the trademark name for dacluzimab and an

anti-Tac antibody, is administered to patients with multiple sclerosis. The "Study of Zenapax" document does not teach co-administration of any IFN-β.

Khoury does not teach a method of administration of IFN-β or an IL-2R antagonist to a subject with multiple sclerosis, but does teach that changes in activated T lymphocyte populations correlate with progression of multiple sclerosis. Specifically, Khoury found a strong correlation between the percentage of $CD25^+$ (i.e. Tac^+) T lymphocytes and the incidence of multiple sclerosis attacks/relapses, as well as the resulting changes in patient disability (see abstract; p. 1187, 2nd column).

Paty and Jacobs teach administration of IFN-β-1b and IFN-β-1a, respectively, to patients suffering from multiple sclerosis. The disclosures of both documents indicate that both IFN-β molecules are effective in treating multiple sclerosis. Paty describes IFN-β-1b-treated patients with decreased brain inflammation, as evidenced by decreases in the number of lesions detected by MRI (abstract, p. 664-665), while Jacobs teaches that IFN-β-1a-treated patients had significantly fewer exacerbations and a decreased number and volume of brain lesions as determined by MRI (abstract).

In the response received on 12/18/2006, the Applicants argue that a combination of agents, each separately effective for treatment of a disease, will not necessarily be effective in treating the disease. The Applicants presented the results of several studies that suggest the combination of different agents does not necessarily result in a superior effect. Thus, the Applicants argue that a reference teaching one type of therapy for multiple sclerosis, such as IFN-β-1b, would not necessarily suggest combination with another reference describing the treatment of multiple sclerosis, such as IFN-β-1a.

These results have been fully considered and are not persuasive. The claims of the instant invention are drawn to methods of treating multiple sclerosis by administration of a combination of IFN-β-1a or IFN-β-1b and an anti-IL-2R antibody. As stated in the previous office action, IFN-β-1a and IFN-β-1b are taught as therapeutic agents for multiple sclerosis by Paty and Jacobs, respectively. The Study of Zenepax document describes treatment of multiple sclerosis with anti-IL-2R antibodies, and Khoury provides further motivation to treat multiple sclerosis by inhibiting/antagonizing the IL-2R. Thus, teachings exist in the prior art that would motivate a skilled artisan to treat multiple sclerosis with IFN-β-1a, IFN-β-1b, and/or anti-IL-2R antibodies. Regarding the Applicants' arguments that the teachings of submitted Exhibits A-C would lead a skilled artisan away from co-administration of IFN-b and anti-IL-2R antibodies, it is

noted that these disclosures are drawn to different diseases, and combinations of different types of therapeutic agents, such as small-molecule drugs.

Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to co-administer IFN-β and anti-IL-2R antibodies for treating subjects with multiple sclerosis because the molecules are taught individually to be effective for treatment. *In re Kerkhoven* (205 USPQ 1069, CCPA 1980) summarizes:

"It is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for the same purpose in order to form a combination that is to be used for the very same purpose: the idea of combining them flows logically from their having been individually taught in the prior art."

It is also noted that none of the "Study of Zenepax" document, Khoury, Paty, or Jacobs disclosures teach away from the use of other therapeutics, and thus one of ordinary skill in the art would have a reasonable expectation of success. Thus, in the absence of evidence that co-administration of IFN-β and anti-IL-2R would fail to effectively treat multiple sclerosis, a skilled artisan would have a reasonable expectation of success in practicing a method that is commensurate in scope with the instant claims.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 20 remains provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-21 and 29-34 of copending Application No. 10/607,598, as set forth on pages 9-10 of the office action mailed on 8/11/2006. In the response received on 12/18/2006, the Applicants did not address this rejection. Accordingly, the rejection is maintained.

Conclusion

No claim is allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BDH
Art Unit 1646

ROBERT S. LANDSMAN, PH.D
PRIMARY EXAMINER